REMARKS

Claims 69, 70, 72, and 74 are pending and under consideration in the application.

35 U.S.C. § 112, first paragraph

The Examiner rejects claims 69, 70, 72, and 74 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled. *See* the Final Action, at page 3, item 5. Specifically, the Examiner alleges that "...the specification, while being enabling for a method of enhancing a nucleic acid polymerase comprising (a) forming a nucleic acid polymerase reaction composition comprising (i) a nucleic acid (ii) at least one nucleic acid polymerase, wherein said polymerase is Pfu DNA polymerase and..., it does not reasonably provide enablement for a method of enhancing a nucleic acid polymerase reaction comprising: forming a nucleic acid polymerase reaction comprising: (i) a nucleic acid and any nucleic acid polymerase and...." *See id.* The Examiner then considers certain factors disclosed in *In re Wands,* 858 F2d 731, 8 USPQ2d 1400 (Fed. Cir. (1988)), and makes certain allegations based on those factors to support her contention that the claims are not enabled. Applicants respectfully traverse.

"The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt,* 537 F.2d 498, 504, 190 U.S.P.Q. 214, 219 (CCPA 1976)." *See* MPEP §2164.01. When additional experimentation is necessary to practice an invention, the Federal Circuit in *Wands*, described eight factors (thereafter known as the "*Wands* factors") to be considered in

determining whether the amount of experimentation would be undue. Here, the Examiner specifically addresses four of the *Wands* factors.

At the outset, applicants assert that the Examiner has not considered all the evidence related to the *Wands* factors in the Examiner's analysis, and therefore, the Examiner's analysis is improper. Specifically, as noted in the MPEP, "[t]he examiner's analysis [of the *Wands* factors] must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. 858 F.2d at 737, 740, 8USPQ2d at 1404, 1407." *See* MPEP §2164.01(a). In her analysis of the *Wands* factors, the Examiner alleges that applicants' only working examples are with Pfu DNA polymerase. *See, e.g.,* the Final Action at page 5, item 5. That is incorrect. In fact, the specification discloses working examples with several other polymerases, including Deep Vent DNA polymerase; JDF3 DNA polymerase; ES4 DNA polymerase; and Vent DNA polymerase, which appear at Example 15, section 2, and in Figure 35. *See, e.g.,* the specification at page 63, lines 3 to 24, and at Figure 35. The Examiner did not consider those examples in her analysis of the *Wands* factors. For that reason alone, applicants assert that the Examiner has not considered all of the evidence related to each of the *Wands* factors. Therefore, the Examiner's enablement analysis is improper.

With regard to the Examiner's allegations concerning the *Wands* factors, applicants will address each factor discussed by the Examiner in turn.

The Quantity of Experimentation Necessary

The Examiner alleges that "[n]owhere in the specification is there an indication that any of the numerous nucleic acid polymerase[s] known in the art..., besides Pfu DNA polymerase, [are] capable of being enhanced when combined in a nucleic acid polymerase composition comprising a polymerase enhancing factor P45 protein or polymerase enhancing factor activity." *See* Final Action at page 5, item 5. With regard to claim 72, the Examiner also alleges that "...the specification provides no teaching wherein any extract, protein, complex, mixture or analog that may have a polymerase enhancing factor activity as claimed in claim 72 is capable of function[ing] in the method for controlling the activity of a polymerase." *See id.* The Examiner then alleges that testing all of the different polymerases and polymerase enhancing factor activities to determine whether they function in the claimed method would be unduly burdensome. *See id.* at page 6, item 5.

Applicants respectfully traverse. Specifically, as noted above, applicants assert that the Examiner is incorrect in asserting that Pfu DNA polymerase is the only DNA polymerase taught by the specification. For example, in Example 15, section 2, applicants discuss enhancing nucleic acid polymerase reaction compositions comprising Deep Vent DNA polymerase, JDF3 DNA polymerase, ES4 DNA polymerase, and Vent DNA polymerase. *See, e.g.,* the specification at page 63, lines 3 to 24. Thus, applicants demonstrated enhancement of nucleic acid polymerase reaction compositions for several different polymerases other than Pfu DNA polymerase.

Furthermore, if one skilled in the art wanted to test whether a reaction composition comprising a particular polymerase worked in a claimed method, one could

do so by running a nucleic acid polymerase reaction (e.g., a PCR reaction) with PEF and the particular polymerase. Such experiments were well within the skill of the art and could probably be completed within a single day. *See, e.g.,* the specification at Example 14, page 60, line 22, which describes performing polymerization reactions in 30 minutes.

With regard to the Examiner's assertions concerning the polymerase enhancing factor activities of claim 72, applicants assert that the specification enables methods for controlling the activity of a polymerase in a nucleic acid polymerase reaction according to claim 72. For example, Example 1, section 2, describes an "'On/Off' assay" using a PEF activity. *See* the specification at page 22, lines 1 to 13. As another example, Applicants investigated the inhibitory action of dUTP in amplification reactions and the ability of PEF to reverse that inhibitory action. See, e.g., the specification at page 52, line 1, to page 55, line 30. Thus, applicants have demonstrated methods for controlling the activity of a polymerase in a nucleic acid polymerase reaction according to claim 72. Furthermore, as pointed out above, if one skilled in the art wanted to test whether a particular polymerase worked in a claimed method with a particular PEF activity, one could do so relatively quickly by running a nucleic acid polymerase reaction with the particular polymerase and the particular PEF activity.

Thus, applicants assert that the quantity of experimentation necessary to practice the invention is low.

The Amount of Direction or Guidance Presented and the Presence or Absence of Working Examples

With regard to the Examiner's contentions concerning (i) the amount of direction or guidance presented and (ii) the presence or absence of working examples, the Examiner alleges that "[t]here is no guidance in the specification for detecting any and every possible extract, protein, complex, mixture of proteins or analogs thereof which may or may not be functional for controlling the activity of a polymerase. Additionally there is no direction or guidance given to substantiate what effect any nucleic acid polymerase would have in the presence of a polymerase enhancing factor P45 protein or polymerase enhancing factor activity without further experimentation for the broad scope of the claims." *See* Final Action at page 6, item 5. With regard to the examples, the Examiner alleges that "[t]he examples beginning at 20 to page 68 lack information concerning using any nucleic acid polymerase known in the art and/or any polymerase enhancing factor activity which may comprise any and every possible extract, protein, protein complex, [or] mixtures." See *id.*

Applicants respectfully traverse. Applicants assert that there is substantial guidance presented regarding the polymerase enhancing factor activities and polymerases used in the claims. Specifically, the specification includes multiple examples of nucleic acid polymerase reactions comprising different polymerases and different PEF activities. For example, the examples describe the use of cell extracts (*See*, e.g., the specification at Example 1, pages 20 to 21); partially-purified column fractions (*See, e.g.,* the specification at Example 3, pages 25 to 26); and purified p45 (*See, e.g.*, the specification at Example 10, section 3, pages 47 to 48). Furthermore,

the specification describes the use of several different polymerases, including Pfu DNA polymerase; Deep Vent DNA polymerase; JDF3 DNA polymerase; ES4 DNA polymerase; and Vent DNA polymerase. *See, e.g.,* the specification at page 63, lines 3 to 24.

Additionally, those examples are all working examples. Furthermore, applicants are not required to provide working examples for all possible combinations of polymerases and polymerase enhancing factor activities to demonstrate which combinations work. *See* MPEP §2164.03 ("The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required.")

Thus, applicants assert that there is substantial guidance in the specification for performing the claimed methods. Furthermore, applicants assert that there are several working examples disclosed in the specification.

The Predictability or Unpredictability of the Art

Finally, the Examiner alleges that "...the results of any screening [of nucleic acid polymerase reaction compositions] or modification thereof is unpredictable since a reasonable expectation of success is limited by a lack of knowledge concerning the [functionality] of all of the nucleic acid molecules and protein molecules [encompassed] by the claimed invention." *See* Final Action at page 7, item 5.

Applicants respectfully traverse. "The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a

change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art." *See* MPEP §2164.03.

In this case, it was routine in the art at the time the application was filed to perform a nucleic acid polymerase reaction. In addition, the specification describes numerous methods of varying certain components of nucleic acid polymerase reaction compositions to optimize the nucleic acid polymerase reactions. *See, e.g.,* the specification at page 2, line 20, to page 5, line 17. Similarly, many different DNA polymerases had been characterized at the time of filing. *See, e.g.,* the article cited by the Examiner in the Final Action, T.A. Brown, *Molecular Biology LabFax,* Biosis Scientific Publishers, Blackwell Scientific Publications, Madison, WI, pages 140 to 153, (December 1991). Based on those known characteristics, one skilled in the art could add or remove DNA polymerases from a nucleic acid polymerase reaction composition while reasonably anticipating the effect of those changes on the nucleic acid polymerase reaction.

Thus, the issue becomes whether one can anticipate the effect of adding (i) p45 or (ii) a polymerase enhancing factor activity to a nucleic acid polymerase reaction composition, wherein the polymerase enhancing factor activity changes the amount of dUTP present or generated during the reaction. However, even if one could not predict the effect of adding a polymerase enhancing factor activity to a nucleic acid polymerase reaction, that unpredictability would not render the claims not enabled because unpredictability of the art is only one factor to be considered in a *Wands* analysis.

Indeed, according to the MPEP, "[t]he amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)." *See* MPEP §2164.03. In this case, as noted above, the amount of guidance provided in the specification is high. Thus, even if one skilled in the art might not be able to predict whether any particular polymerase or polymerase enhancing factor activity would work in one of the claimed methods, that particular polymerase or polymerase enhancing factor activity could be tested by running a relatively predictable nucleic acid polymerase reaction, such as a PCR reaction, with the particular polymerase or polymerase enhancing factor following the teachings of the specification. Thus, applicants assert that even if the art is unpredictable, the claims are still enabled.

Accordingly, applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §112, first paragraph, rejection of claims 69, 70, 72, and 74.

Applicants respectfully submit that the application is in condition for allowance. In the event the Examiner does not find the claims allowable, Applicants request that the Examiner contact the undersigned at (650) 849-6658 to set up an interview.

If there is any fee due in connection with the filing of this Amendment, please charge the fee to Deposit Account No. 06-0916.

Respectfully submitted,

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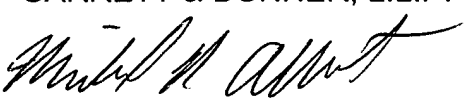
By: 

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